Docket No.: PF-0544 USN

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By: _____ Printed: Katherine Stofer

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Bandman et al.

Title:	HUMAN OXIDOREDUCTASE PROTEINS		
Serial No.:	09/719,601	Filing Date:	February 19, 2002
Examiner:	To Be Assigned	Group Art Unit:	1645

Box Non-Fee Amendment
Commissioner for Patents
Washington, D.C. 20231

RESPONSE TO RESTRICTION REQUIREMENT UNDER 35 U.S.C. 121

Sir:

This paper is responsive to the Restriction Requirement and Request for Election dated **December 31, 2002**, setting a **one (1) month** term for response. Prior to examination of the application, please amend the specification of the above-identified application as listed below.

IN THE CLAIMS

Please cancel claims 1-20 without prejudice or disclaimer.

Please add the following new claims 21-40.

For the Examiner's convenience, all pending claims are listed below. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

21. (New) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-6,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-6,

c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-6, and

d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

22. (New) An isolated polypeptide of claim 21 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

23. (New) An isolated polynucleotide encoding a polypeptide of claim 21.

24. (New) An isolated polynucleotide encoding a polypeptide of claim 22.

25. (New) An isolated polynucleotide of claim 24 comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12.

26. (New) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 23.

27. (New) A cell transformed with a recombinant polynucleotide of claim 26.

28. (New) A method of producing a polypeptide of claim 21, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant

polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 21, and

b) recovering the polypeptide so expressed.

29. (New) A method of claim 28, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

30. (New) An isolated antibody which specifically binds to a polypeptide of claim 21.

31. (New) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

32. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

33. (New) A method of claim 32, wherein the probe comprises at least 60 contiguous nucleotides.

34. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

35. (New) A composition comprising a polypeptide of claim 21 and a pharmaceutically acceptable excipient.

36. (New) A composition of claim 35, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

37. (New) A method of screening for a compound that specifically binds to the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 21 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 21.

38. (New) A method of screening for a compound that modulates the activity of the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 21,

b) assessing the activity of the polypeptide of claim 21 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 21 in the presence of the test compound with the activity of the polypeptide of claim 21 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 21 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 21.

39. (New) A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 25, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

40. (New) A method of assessing toxicity of a test compound, the method comprising:

a) treating a biological sample containing nucleic acids with the test compound,

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 31 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 31 or fragment thereof,

c) quantifying the amount of hybridization complex, and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

REMARKS

Justification for the amendments is as follows. Amendment of the claims and addition of the new claims serve to further clarify the subject matter which applicants consider to be the invention. New claims 23-29 and 31 are drawn to polynucleotides, expression vectors, host cells, and methods of producing a polypeptide and replace original claims 3-12, while new claims 21-22, 30, and 35-36 are drawn to polypeptides, antibodies, and compositions comprising the polypeptide and replace claims 1-2, 13, and 14. New claims 32-24 are drawn to methods of detection of polynucleotides and replace claims 19-20. New claims 37 and 38, which are drawn to methods of identifying compounds that bind to and modulate the activity of the polypeptide, are supported in the specification at, e.g., page 43, lines 10-22, and page 57, lines 22-27. New claims 39 and 40, drawn to methods of testing compounds for effectiveness in altering polynucleotide expression and for toxicity, are supported in the specification at, e.g., page 41, lines 7-20, and page 42, lines 6-11. No new matter is added by any of these amendments.

Restriction Requirement

In the Restriction Requirement, the Examiner requested Applicants to elect one of the following inventions:

Group I (claims 1-2, 13, and 17) drawn to a polypeptide, pharmaceutical composition, and method of treatment.

Group II (claims 3-12) drawn to DNA, vector, host cell, and a process.

Group III (claim 14) drawn to an antibody.

Group IV (claim 15) drawn to a purified agonist.

Group V (claim 16) drawn to a purified antagonist.

Group VI (claim 18) drawn to a method of diagnosis using an antagonist.

Group VII (claims 19-20) drawn to a method of detecting a polynucleotide by hybridization.

Applicants hereby elect, with traverse, to prosecute Group II, which includes and is drawn to claims 23-29 and 31 (replacing original claims 3-12). Further, Applicants elect, with traverse, to prosecute claims related to the polynucleotide sequences encoding the

polypeptide sequence of SEQ ID NO:5, which sequences include SEQ ID NO:11, and which sequences read on claims 23-29 and 31. Applicants reserve the right to prosecute the subject matter of non-elected claims in subsequent divisional applications. Applicants traverse both the restriction requirement and the obligation to elect a single sequence for prosecution which were imposed in the Office Action mailed December 31, 2002 for at least the following reasons.

The unity of invention standard *must* be applied in national stage applications

Section 1850 of the Manual of Patent Examining Procedure (original 8th edition, published August, 2001) (hereinafter "MPEP") provides:

> ... [W]hen the Office considers international applications ... during the national stage as a Designated or Elected Office under 35 U.S.C. 371, PCT Rule 13.1 and 13.2 will be followed when considering unity of invention of claims of different categories without regard to the practice in national applications filed under 35 U.S.C. 111....
>
> In applying PCT Rule 13.2 to ... national stage applications under 35 U.S.C. 371, examiners should consider for unity of invention all the claims to different categories of invention in the application and permit retention in the same application for searching and/or preliminary examination, claims to the categories which meet the requirements of PCT Rule 13.2....

Id at page 1800-60 to -61.

MPEP section 1893.03(d) reiterates the Examiner's obligation to apply the Unity of Invention standard PCT Rule 13.2 instead of U.S. restriction/election of species practice:

> Examiners are reminded that unity of invention (not restriction) practice is applicable ... in national stage (filed under 35 U.S.C. 371) applications.

Id at page 1800-149, column 1.

Specific provisions of the Administrative Regulations Under the PCT and the corresponding provisions of the MPEP strongly support a finding of unity of invention among all of the claims in the present case

Unity of Invention is accepted as between claims to polypeptide sequences and claims to the polynucleotide sequences which encode them

Example 17, Part 2 of Annex B to the Administrative Instructions Under the PCT provides that unity of invention is accepted as between claims to polypeptide sequences and claims to polynucleotide

sequences encoding those polypeptides. Those Examples are cited in MPEP section 1893.03(d) at page 1800-149, column 2 ("[n]ote also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions...")

Thus, in the present case, unity of invention exists at least as between claims drawn to polypeptide sequences SEQ ID NO:1-6 (*i.e.*, claims 21, 22, 35, and 36) and as to claims drawn to polynucleotide sequences which encode those polypeptides (*i.e.*, claims 23-26 and 31).

Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to claims 21-26, 31, 35, and 36, and examine those claims in a single application.

Unity of invention exists with respect to dependent claims in the same claim category as the independent claim from which they depend

MPEP section 1850(A) and 1893.03(d), which recite the provisions of paragraph (c) of Part 1 (entitled "Instructions Concerning Unity of Invention") of Annex B (entitled "Unity of Invention") to the Administrative Instructions Under the PCT, provides:

> **(A) Independent and Dependent Claims.**
>
> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of another claim and is in the same category of claim as that other claim (the expression "category of claim" referring to the classification of claims according to the subject matter of the invention claimed for example, product, process, use or apparatus or means, etc.).
>
> (i) If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention....

See MPEP section 1850(A) at page 1800-61. See also MPEP Appendix AI at page 53.

In the present case, claims 22-27, 35 and 36, all of which depend from claim 21, are all directed to compositions of matter, *i.e.*, to products. All of these claims contain all of the features of the independent claim. Further, as discussed above, there is unity of invention as between claim 21 and claim 31.

Thus, it is improper to restrict claims 21, 22, 35 and 36 (replacing original claims 1, 2, and 13) from claims 23-27 and 31 (replacing original claims 3-12), as the Examiner has done. Therefore, Applicants respectfully request that the Examiner withdraw the Restriction Requirement at least as to the composition of matter claims, and that at least those claims be considered together in a single application.

Unity of invention exists as between all of Applicants' claims

MPEP 1850 provides:

> Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more special technical features. The term "special technical features" is defined as meaning those technical features that define a contribution which each of the inventions considered as a whole, makes over the prior art. The determination is made based on the contents of the claims as interpreted in light of the description and drawings. Annex B also contains examples concerning unity of invention.

Id at page 800-61.

MPEP 1893.03(d) similarly provides:

> A group of inventions is considered linked to form a single general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression special technical features is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. For example, a corresponding technical feature is exemplified by a key defined by certain claimed structural characteristics which correspond to the claimed features of a lock to be used with the claimed key. Note also examples 1-17 of Annex B Part 2 of the PCT Administrative Instructions as amended July 1, 1992 contained in Appendix AI of the MPEP.

Id at page 1800-149.

In the present case, unity of invention exists among all of Applicants' claims. The claimed polypeptide sequences and the claimed polynucleotide sequences encoding them are corresponding technical features which are common to all of Applicants' claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application.

The claimed polypeptide sequences, and the claimed polynucleotide sequences encoding those polypeptide sequences, are corresponding technical features that are common to all of Applicants' claims and that serve to technically interrelate them

Applicants' claims recite *inter alia* the polypeptides SEQ ID NO:1-6, and polynucleotides encoding those polypeptides, which sequences include the polynucleotide sequences SEQ ID NO:7-12. See Table 1 of the specification. Applicants respectfully submit that the claimed polypeptide sequences SEQ ID NO:1-6, and the claimed polynucleotide sequences encoding them, are corresponding technical features, given that the former are encoded by the latter, and conversely, the latter encode the former.

Further, the claimed polypeptide and corresponding polynucleotide sequences are common to all of Applicants' claims, given that each claim refers to one or both either explicitly or implicitly, by virtue of depending from a claim which makes an explicit reference to the claimed sequences.

Moreover, the claimed polypeptide and corresponding polynucleotide sequences serve to technically interrelate all of Applicants' claims. Applicants' composition of matter claims (21-27, 30, 31, 35 and 36) are drawn to either the sequences themselves (21 and 22, drawn to polypeptide sequences, and 23-25 and 31, drawn to polynucleotide sequences), to compositions of matter which comprise the sequences as one element (26-27, drawn to recombinant polynucleotide sequences and transformed cells, respectively, and 35 and 36, drawn to pharmaceutical compositions), or to compositions of matter wherein the claimed sequences functionally limit the claimed subject matter (claim 30, drawn to antibodies which specifically bind a polypeptide of claim 21).

In Applicants' method claims (28, 29, 32-34, and 37-40), the claimed sequences serve as either the product of the claimed method (claims 28 and 29, drawn to a method of polypeptide production) and/or as a reagent for performing the method (claims 37 and 38, drawn, respectively, to methods of screening for compounds which specifically bind, or compounds which modulate the activity of, a polypeptide of claim 21; and claims 32-34, 39, and 40, drawn, respectively, to methods of detecting a target polynucleotide in a sample, a method of screening for compounds which alter the expression of a target polynucleotide, and a method for assessing toxicity of a test compound).

Therefore, the claimed polypeptide and polynucleotide sequences are corresponding technical features which are common to all of Applicants' claims, and which serve to technically interrelate them.

In sum, the claimed polypeptide sequences and the claimed polynucleotide sequences which encode them are corresponding technical features which are common to all of Applicants claims, which serve to technically interrelate all of Applicants' claims, and which define the contribution over the prior art made by each of them. Thus, Applicants' claims are linked to form a single general inventive concept, and Applicants are therefore entitled to prosecute all of their pending claims in a single national stage application. Withdrawal of the restriction requirement in the present case is therefore respectfully requested.

In the event that the Examiner does not apply the unity of invention standard to this national phase application, Applicants note that the invention encompassed by claims 32-34 (replacing claims 7 and 8 of Group III) and claims 39 and 40 are drawn to methods of use of the polynucleotides of Group II, and should be examined together. These method claims recite a product (i.e., a polynucleotide), which is of the same scope as the claimed polynucleotides being searched by the Examiner. Therefore, it would not be an undue burden on the Examiner to examine these method claims since the searches for the claimed polynucleotides and these method claims would substantially overlap.

In addition, the method claims 32-34, 39, and 40 are entitled to rejoinder upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products. See also M.P.E.P. 821.04 as follows.

> Where product and process claims drawn to independent and distinct inventions are presented in the same application, applicant may be called upon under 35 U.S.C. 121 to elect claims to either the product or process. . . The claims to the nonelected invention will be withdrawn from further consideration under 37 C.F.R. 1.142. . . . However, if applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claim will be rejoined.

The Election of Species Requirement

Applicants elect, with traverse, to prosecute claims related to the polynucleotide sequences encoding the polypeptide sequence of SEQ ID NO:5, which sequences include SEQ ID NO:11. Those polynucleotide sequences read on claims 23-29 and 31. Applicants traverse the Election of Species Requirement for at least the following reasons.

The Examiner's attention is directed to the Patent Office's own requirements for Markush practice, set forth in the 7th edition of the M.P.E.P. (July 1998) at § 803.02 regarding restriction requirements in Markush-type claims:

PRACTICE RE MARKUSH-TYPE CLAIMS

> If the members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.
>
> Since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), **it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, **unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility**.
>
> This subsection deals with Markush-type generic claims which include a plurality of alternatively usable substances or members. In most cases, a recitation by enumeration is used because there is no appropriate or true generic language. A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the

Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration.

As an example, in the case of an application with a Markush-type claim drawn to the compound C-R, wherein R is a radical selected from the group consisting of A, B, C, D, and E, the examiner may require a provisional election of a single species, CA, CB, CC, CD, or CE. The Markush-type claim would then be examined fully with respect to the elected species and any species considered to be clearly unpatentable over the elected species. If on examination the elected species is found to be anticipated or rendered obvious by prior art, the Markush-type claim and claims to the elected species shall be rejected, and claims to the nonelected species would be held withdrawn from further consideration. As in the prevailing practice, a second action on the rejected claims would be made final.

On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. The prior art search, however, will not be extended unnecessarily to cover all nonelected species. Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry. [emphasis added]

As can be seen from the above, it is clear that the present Restriction Requirement does not meet the Patent Office's own requirements.

First, if the number of "members of the Markush group are **sufficiently few in number or so closely related** that a search and examination of the entire claim can be made without serious burden, the examiner must examine all claims on the merits, even though they are directed to independent and distinct inventions. **In such a case, the examiner will not follow the procedure described below and will not require restriction.**" Withdrawal of the restriction requirement as between the specific sequences each in the claims is required on that basis alone.

Second, "**it is improper for the Office to refuse to examine that which applicants regard as their invention**, unless the subject matter in a claim lacks unity of invention. ... Broadly, **unity of**

invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." Clearly, the sequences of the instant invention share both a common utility and structural homology, based on their classification as human oxidoreductase proteins.

Third, even if the claims could be considered to be "Markush-type generic claims which include a plurality of alternatively usable substances or members," it is further noted that the M.P.E.P states that "A Markush-type claim can include independent and distinct inventions. This is true where two or more of the members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. 103 with respect to the other member(s). In applications containing claims of that nature, **the examiner may require a provisional election of a single species** prior to examination on the merits." This clearly applies in the present case.

Finally, the Examiner's attention is directed to the M.P.E.P. at § 803.04 (Restriction - Nucleotide Sequences, EXAMPLES OF NUCLEOTIDE SEQUENCE CLAIMS) which states:

> Applications claiming more than ten individual independent and distinct nucleotide sequences in alternative form, such as set forth in example (A), will be subject to a restriction requirement. Only the ten nucleotide sequences selected in response to the restriction requirement and any other claimed sequences which are patentably indistinct therefrom will be examined.
>
> Applications claiming only a combination of nucleotide sequences, such as set forth in example (B), will generally not be subject to a restriction requirement. The presence of one novel and nonobvious sequence within the combination will render the entire combination allowable. The combination will be searched until one nucleotide sequence is found to be allowable. The order of searching will be chosen by the examiner to maximize the identification of an allowable sequence. If no individual nucleotide sequence is found to be allowable, the examiner will consider whether the combination of sequences taken as a whole renders the claim allowable.

Therefore, it is respectfully submitted that, upon searching and examining SEQ ID NO:11 and finding no prior art over which SEQ ID NO:11 can be rejected, the Examiner must extend the search of the Markush-type claim to include the five additional non-elected species.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. 09-0108.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1-20 have been canceled.

Claims 21-40 have been added:

21. (New) An isolated polypeptide selected from the group consisting of:

a) a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-6,

b) a polypeptide comprising a naturally occurring amino acid sequence at least 90% identical to an amino acid sequence selected from the group consisting of SEQ ID NO:1-6,

c) a biologically active fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-6, and

d) an immunogenic fragment of a polypeptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

22. (New) An isolated polypeptide of claim 21 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

23. (New) An isolated polynucleotide encoding a polypeptide of claim 21.

24. (New) An isolated polynucleotide encoding a polypeptide of claim 22.

25. (New) An isolated polynucleotide of claim 24 comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12.

26. (New) A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 23.

27. (New) A cell transformed with a recombinant polynucleotide of claim 26.

28. (New) A method of producing a polypeptide of claim 21, the method comprising:

a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 21, and

b) recovering the polypeptide so expressed.

29. (New) A method of claim 28, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

30. (New) An isolated antibody which specifically binds to a polypeptide of claim 21.

31. (New) An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12,

b) a polynucleotide comprising a naturally occurring polynucleotide sequence at least 90% identical to a polynucleotide sequence selected from the group consisting of SEQ ID NO:7-12,

c) a polynucleotide complementary to a polynucleotide of a),

d) a polynucleotide complementary to a polynucleotide of b), and

e) an RNA equivalent of a)-d).

32. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions

whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and

b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

33. (New) A method of claim 32, wherein the probe comprises at least 60 contiguous nucleotides.

34. (New) A method of detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 31, the method comprising:

a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and

b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

35. (New) A composition comprising a polypeptide of claim 21 and a pharmaceutically acceptable excipient.

36. (New) A composition of claim 35, wherein the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1-6.

37. (New) A method of screening for a compound that specifically binds to the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under suitable conditions, and

b) detecting binding of the polypeptide of claim 21 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 21.

38. (New) A method of screening for a compound that modulates the activity of the polypeptide of claim 21, the method comprising:

a) combining the polypeptide of claim 21 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 21,

b) assessing the activity of the polypeptide of claim 21 in the presence of the test compound, and

c) comparing the activity of the polypeptide of claim 21 in the presence of the test compound with the activity of the polypeptide of claim 21 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 21 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 21.

39. (New) A method of screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 25, the method comprising:

a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,

b) detecting altered expression of the target polynucleotide, and

c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

40. (New) A method of assessing toxicity of a test compound, the method comprising:

a) treating a biological sample containing nucleic acids with the test compound,

b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 31 under conditions whereby a specific hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 31 or fragment thereof,

c) quantifying the amount of hybridization complex, and

d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.